

Low Right Care

Reducing Overuse and Underuse

Anticoagulation in Older Adults

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Case Scenario

Mr. H is an 84-year-old man with well-controlled hypertension and hyperlipidemia. He recently presented to the emergency department with anxiety symptoms, shortness of breath, and palpitations. A clinical examination found an irregular heart rhythm of 140 to 160 beats per minute. An electrocardiogram (ECG) showed atrial fibrillation with no acute ST-T wave changes. After Mr. H received an intravenous dose of a beta blocker, his heart rate quickly decreased to the 80s, and his symptoms resolved. However, a repeat ECG showed that he was in atrial fibrillation. He was admitted for telemetry monitoring, and an oral beta blocker and intravenous heparin were initiated. Laboratory tests showed no evidence of ischemia, anemia, electrolyte imbalance, or thyroid dysfunction. An echocardiogram showed calcification of the aortic and mitral valves but no stenosis or significant regurgitation. A cardiologist recommended prescribing a direct oral anticoagulant to prevent an embolic stroke. However, Mr. H's primary care physician is concerned about the risks of anticoagulation because of recent functional decline in the patient, including a slowing of his gait without any falls.

Clinical Commentary

Atrial fibrillation is the most common cardiac arrhythmia, occurring in an estimated 2.7 million to 6.1 million people in the United States.¹ Approximately 9% of people 65 years and older have this condition, and it occurs more often in women.² Risk factors include hypertension, diabetes mellitus, ischemic heart disease, and older age. Each

TAKE-HOME MESSAGES FOR RIGHT CARE

Risk stratification is essential to identify patients who may benefit the most from anticoagulation therapy.

Evaluate comorbidities, medication use, risk of falls, and risk of bleeding for evidence-based decision-making.

Patient-centered, shared decision-making discussions between the physician and patient are essential to evaluate the benefits and risks of anticoagulation.

year atrial fibrillation causes more than 750,000 hospital admissions and more than 130,000 deaths, often associated with strokes.³ An estimated 15% to 20% of strokes occur in patients with underlying atrial fibrillation.^{4,5}

The use of warfarin (Coumadin) and direct oral anticoagulants such as rivaroxaban (Xarelto), apixaban (Eliquis), and dabigatran (Pradaxa) to prevent strokes is the first-line treatment for younger patients with atrial fibrillation. However, the use of direct oral anticoagulants in older people is problematic because of a higher risk of morbidity and mortality from gastrointestinal and intracerebral bleeding, which can be exacerbated by falls.

Practice guidelines recommend risk stratification with the CHA₂DS₂-VASc tool (congestive heart failure; hypertension; age 75 years or older [doubled]; diabetes mellitus; prior stroke, transient ischemic attack, or thromboembolism [doubled]; vascular disease; age 65 to 74 years; sex category; <https://www.mdcalc.com/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk>) to identify patients who could benefit from anticoagulation therapy; however, there is a modest predictive ability for ischemic stroke.⁶⁻⁸ Some physicians use the CHA₂DS₂-VASc tool to determine whether to initiate anticoagulation therapy without considering the patient's functional status and bleeding risk, which is not recommended. Bleeding risk scores such as HAS-BLED (hypertension, abnormal renal and liver function, stroke history, bleeding risk, labile international normalized ratio, elderly [older than 65 years], drugs and alcohol use; <https://www.mdcalc.com/has-bleed-score-major-bleeding-risk>) may help assess risk but have limited predictive power.

See related editorial on page 713.

Low Institute Right Care Alliance is a grassroots coalition of clinicians, patients, and community members organizing to make health care institutions accountable to communities and to put patients, not profits, at the heart of health care.

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 719.

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COST OF COMMON ANTICOAGULANTS

A 2007 Cochrane review evaluated high-quality placebo-controlled studies comparing the benefits and risks of anticoagulation in atrial fibrillation. Participants were younger (average age 69 years) and had less comorbidity than the general population. After two years, patients taking warfarin experienced 17 out of 1,000 fewer strokes (number needed to treat [NNT] = 59) and five out of 1,000 fewer disabling or fatal strokes (NNT = 200). This distinction is essential because most studies assess only the reduction of all strokes, some of which are mild or quickly resolve. Compared with those who received placebo, participants who were treated with warfarin experienced 40 out of 1,000 more severe bleeds (number needed to harm [NNH] = 25), six of which were fatal, and six out of 1,000 more developed hemorrhagic strokes (NNH = 83 for fatal bleeds and hemorrhagic strokes combined). There was no difference in all-cause mortality.⁹

Few older people are included in randomized controlled trials of anticoagulation; therefore, there are limited data about risks in this population.^{10,11}

A 2018 cohort study examined the risks and benefits of anticoagulation in people 90 years and older. Fifteen out of 1,000 averted strokes with anticoagulation therapy (NNT = 67), and the rate of averting a stroke was similar between warfarin and direct oral anticoagulants. In the direct oral anticoagulant arm, four out of 1,000 had a hemorrhagic stroke vs. 16 out of 1,000 in the warfarin arm. In each group using anticoagulation therapy, approximately 60 out of 1,000 participants had major bleeds.¹²

It is unclear how often older people with comorbidities that would increase the risk of bleeding (e.g., prior bleeding events, prior reactions to anticoagulation, falls, use of antiplatelet agents) are included in anticoagulation trials. Results of studies evaluating the effect of these factors are inconsistent; therefore, clinicians must use their judgment about benefits and risks in this population.¹³ One study of patients who fall often found that patients taking anticoagulants had a similar rate of bleeding as patients not taking anticoagulants; however, patients who did bleed had a higher rate of death if they were taking anticoagulants (146 out of 1,000 excess deaths; NNH = 7).¹⁴ It is important to know how well an older patient can tolerate warfarin and whether they can take medication consistently because these factors will affect possible harms.

Drug	Dosage	Cost*
Warfarin (Coumadin)	Dose is individualized based on international normalized ratio	\$13 (\$75) for 30 5-mg tablets
Apixaban (Eliquis)	Start with 10 mg twice per day for one week, then 5 mg twice per day	— (\$250) for 30 5-mg tablets
Betrixaban (Bevyxxa)	Single dose of 160 mg followed by 80 mg once per day	— (\$500) for 30 80-mg capsules
Dabigatran (Pradaxa)	150 mg twice per day (CrCl > 30 mL per minute per 1.73 m ² [0.50 mL per second per m ²]) 75 mg twice per day (CrCl = 15 to 30 mL per minute per 1.73 m ² [0.25 to 0.50 mL per second per m ²])	— (\$225) for 30 150-mg capsules
Edoxaban (Savaysa)	60 mg per day (CrCl > 95 mL per minute per 1.73 m ² [1.59 mL per second per m ²]) 30 mg per day (CrCl = 15 to 50 mL per minute per 1.73 m ² [0.25 to 0.83 mL per second per m ²])	— (\$400) for 30 60-mg tablets
Rivaroxaban (Xarelto)	20 mg per day (CrCl > 50 mL per minute per 1.73 m ²) 15 mg per day (CrCl ≤ 50 mL per minute per 1.73 m ²)	— (\$475) for 30 20-mg tablets

CrCl = creatinine clearance.

*—Estimated lowest GoodRx price of one month's treatment. Actual cost will vary with insurance and by region. Generic price listed first; brand name in parentheses. Information obtained at <https://www.goodrx.com> (accessed March 17, 2020; zip code 66211).

Studies have shown that direct oral anticoagulants are at least as effective as warfarin.¹¹ Comparative risks of bleeding complications are mixed, with some studies showing decreased rates of intracerebral hemorrhage and others showing a slightly increased risk of gastrointestinal bleeding in patients taking direct oral anticoagulants.¹⁵⁻²¹ When necessary, vitamin K can be used to reverse the effects of warfarin. Two medications are U.S. Food and Drug Administration–approved for reversing the effects of direct oral anticoagulants in patients who experience life-threatening bleeding or require emergency surgery. Andexanet alfa (Andexxa) should be used for patients taking apixaban, rivaroxaban, or edoxaban (Savaysa). Idarucizumab (Praxbind) should be used for patients taking dabigatran.²²

Patient Perspective

Members of the public are often concerned about the risk of bleeding from anticoagulants by observing the experiences of those around them. Shared decision-making after discussing the pros and cons of different options is essential in a situation in which the answers are not always clear. Patients should be made aware of data that compare the benefits

and risks of anticoagulation therapy. The physician should also be prepared to discuss nonpharmacologic strategies or strategies that the patient may have learned about on the internet, such as dietary changes or magnesium supplementation. Also, detailed discussions of the incidence of stroke vs. bleeding or overall mortality are not likely to be readily available online. The same is true of the risks inherent in a bleeding episode and the differences between anticoagulants. What are the benefits of monitored vs. unmonitored anticoagulation? What sort of events (e.g., a fall) can precipitate bleeding? How safe is surgery for a patient taking anticoagulants, and how safe and effective is reversal of the anticoagulant? Even informed patients need an objective and trusted professional to filter and explain their options, keeping in mind that important uncertainties exist.

Primary care physicians can help bridge the gap between theory and reality by conveying a thoughtful assessment of possible outcomes and preventive measures. The pressure to administer anticoagulants to large subpopulations of patients assumes that what is good for the majority is good for all and that reducing a single risk will reduce a patient's overall risk. The goal of patients is their global well-being, a goal that does not necessarily align with the optimal end point for each of their medical conditions. It is the fundamental role of the primary care physician to balance these conflicting concerns.

Resolution of Case

Mr. H has a CHA₂DS₂-VASC score of 3 because of his hypertension (one point) and age older than 75 years (two points), indicating a high risk of stroke.⁶ Mr. H and his primary care physician had a shared decision-making conversation. Mr. H has an 8% annual risk of stroke, with less than one-half of that being a risk of a disabling or fatal stroke.^{1,2,9,12} They discussed the costs of medications and potential adverse effects and the need for laboratory testing with warfarin. They also considered his age and recent functional decline, which, if complicated by a fall, could result in severe intracranial bleeding. Together they decided that Mr. H would continue to take the beta blocker to control his heart rate, and he would abstain from anticoagulation therapy and consider taking a daily aspirin as an alternative.

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References

- Centers for Disease Control and Prevention. Atrial fibrillation. Accessed November 10, 2019. https://www.cdc.gov/dhdsdp/data_statistics/factsheets/fs_atrial_fibrillation.htm
- January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation [published correction appears in *J Am Coll Cardiol*. 2014;64(21):2305-2307]. *J Am Coll Cardiol*. 2014;64(21):e1-e76.
- Gómez-Outes A, Lagunar-Ruiz J, Terleira-Fernández AI, et al. Causes of death in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2016;68(23):2508-2521.
- Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association [published corrections appear in *Circulation*. 2015;131(24):e535 and *Circulation*. 2016;133(8):e417]. *Circulation*. 2015;131(4):e29-e322.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991;22(8):983-988.
- Maheshwari A, Norby FL, Roetker NS, et al. Refining prediction of atrial fibrillation-related stroke using the P2-CHA₂DS₂-VASC score. *Circulation*. 2019;139(2):180-191.
- American Academy of Family Physicians. Clinical practice guideline: atrial fibrillation. Accessed March 15, 2020. <https://www.aafp.org/patient-care/clinical-recommendations/all/atrial-fibrillation.html>
- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. *Circulation*. 2019;140(2):e125-e151.
- Aguilar MI, Hart R, Pearce LA. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischemic attacks. *Cochrane Database Syst Rev*. 2007;(3):CD006186.
- Ebell MH. Evaluating the benefits and harms of anticoagulation in patients with atrial fibrillation. *Am Fam Physician*. 2018;98(12):751-753. Accessed March 10, 2020. <https://www.aafp.org/afp/2018/1215/p751.html>
- Wigle P, Hein B, Bernheisel CR. Anticoagulation: updated guidelines for outpatient management. *Am Fam Physician*. 2019;100(7):426-434. Accessed March 10, 2020. <https://www.aafp.org/afp/2019/1001/p426.html>
- Chao TF, Liu CJ, Lin YJ, et al. Oral anticoagulation in very elderly patients with atrial fibrillation: a nationwide cohort study. *Circulation*. 2018;138(1):37-47.
- Seelig J, Pisters R, Hemels ME, et al. When to withhold oral anticoagulation in atrial fibrillation – an overview of frequent clinical discussion topics. *Vasc Health Risk Manag*. 2019;15:399-408.
- Chiu AS, Jean RA, Fleming M, et al. Recurrent falls among elderly patients and the impact of anticoagulation therapy. *World J Surg*. 2018;42(12):3932-3938.
- Sharma M, Cornelius VR, Patel JP, et al. Efficacy and harms of direct oral anticoagulants in the elderly for stroke prevention in atrial fibrillation and secondary prevention of venous thromboembolism: systematic review and meta-analyses. *Circulation*. 2015;132(3):194-204.
- Mitchell A, Watson MC, Welsh T, et al. Effectiveness and safety of direct oral anticoagulants versus vitamin K antagonists for people aged 75 years and over with atrial fibrillation: a systematic review and meta-analyses of observational studies. *J Clin Med*. 2019;8(4):E554.
- Bai Y, Guo SD, Deng H, et al. Effectiveness and safety of oral anticoagulants in older patients with atrial fibrillation: a systematic review and meta-regression analysis. *Age Ageing*. 2018;47(1):9-17.
- Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet*. 2014;383(9921):955-962.
- Vinogradova Y, Coupland C, Hill T, et al. Risks and benefits of direct oral anticoagulants versus warfarin in a real work setting: cohort study in primary care [published correction appears in *BMJ*. 2018;363:k4413]. *BMJ*. 2018;362:k2505.
- Graham DJ, Baro E, Zhang R, et al. Comparative stroke, bleeding, and mortality risks in older Medicare patients treated with oral anticoagulants for nonvalvular atrial fibrillation. *Am J Med*. 2019;132(5):596-604.
- Xian Y, Xu H, O'Brien EC, et al. Clinical effectiveness of direct oral anticoagulants vs warfarin in older patients with atrial fibrillation and ischemic stroke: findings from the patient-centered research into outcomes stroke patients prefer and effectiveness research (PROSPER) Study. *JAMA Neurol*. 2019;76(10):1192-1202.
- Desai NR, Cornutt D. Reversal agents for direct oral anticoagulants: considerations for hospital physicians and intensivists. *Hosp Pract (1995)*. 2019;47(3):113-122. ■